



# Relationships between HIV spread and evolution examined

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Thomas Leitner of the Lab's Theoretical Biology and Biophysics group and collaborators are investigating the development of HIV from the point of contraction onwards. They are examining the relationships between the spread of the virus in a population (epidemiology) and the evolution of the virus (phylogenetics).

The genetic evolution of HIV in infected humans means that unique HIV populations are manifest in each infected individual, which change over time. This evolutionary process leaves a footprint of the transmission history in the genetic material of the virus. The researchers aim to utilize the HIV genetic footprint in mathematical models to reconstruct accurately how epidemics spread. The model systems could be used to predict the effects of intervention campaigns. The project has generated 10 papers, and recently the journals PLoS ONE and Epidemics have published the research.

## Significance of the research

The scientists' project, "Reconstructing HIV Epidemics from HIV Phylogenetics" examines the likelihood of one individual with HIV infecting another. The project also seeks to establish a model that accurately reflects how HIV spreads among the wider population. Such a model would be useful in investigating outbreaks or to plan intervention campaigns.

Other researchers have simulated epidemics using differential equation-based models, which predict overall trends. They cannot study individuals in populations. Los Alamos has developed a hybrid agent-based model that makes it easier to simulate social network structures in which HIV spreads. The "hybrid" component comes from the fact that the team models the uninfected population using traditional differential equations; this is done for computational speed, because the agent-based component is much more demanding. Once a person is infected, he/she becomes an agent, and the model starts following their behavior individually, as well as the HIV evolution within them. This new modeling approach distinguishes between susceptible and infected individuals to capture the full infection history, including contact tracing data for infected individuals. The uninfected individuals are modeled at a population level and stratified by transmission risk and social group. The social network in this model forms—and can change—during the simulation. Thus, the model is much more realistic than traditional models.

Those who have the infection are often unable to establish how many susceptible people they may have had contact with during the infectious period of the disease. Many HIV infections go unnoticed, and diagnosis therefore often occurs long after

the infection is contracted. The research team developed a biomarker model that estimates how long ago a newly diagnosed patient was infected. By determining when the infection was transmitted at the time of diagnosis, Leitner hopes it will be possible to estimate incidence accurately.

### **Research achievements**

The researchers have shown that in fast HIV epidemics—such as that among individuals injecting themselves with drugs—HIV evolution is slow, resulting in little diversification at the population level. Meanwhile, slower-spreading epidemics display more HIV evolution over the same amount of time. What happens in individual transmissions from person to person has large population effects. The reason for this inverse effect lies in the time from infection to further transmission. If infected people transmit HIV further within the early stages, the virus has diversified little and at a slower rate than if further transmissions occur later in the chronic stage.

The team has applied their hybrid mathematical model to the HIV epidemic in Latvia, based on information obtained from the Infectology Center of Latvia. It has also used phylogenetic analyses to examine the spread of HIV-1 in the country between 1987 and 2010. The group tracked infected individuals and followed their transmission histories. The model demonstrated a heterogeneous spread in the population. Small groups of people sharing the same transmission risks may increase the spread of the epidemic locally, because these small groups enhance the probability of infected individuals finding contacts for transmission. An epidemic spreads more widely when infected individuals leave these local clusters and interact with other people. The composition and interactions among these different social groups can influence the overall dynamics of the epidemic, as well as the virus diversification patterns. Conversely, observed viral diversity can prove informative when investigating epidemiological clusters.

### **The research team**

Researchers include Leitner, Frederik Graw, Ruy M. Ribeiro and Helena Skar of T-6 and Jan Albert of the Karolinska Institute and Karolinska University Hospital. The National Institutes of Health funded the research, which supports the Lab's Global Security mission area and the Information, Science, and Technology science pillar.

***Caption for image below:*** Epidemic dynamics in the Latvian injecting drug users and related heterosexual population. Dynamics were inferred using HIV-1 sequence data and a phylogenetic framework.

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